



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/522,171

11/04/2005

Henrik Pedersen

PEDERSEN11

9244

1444 7590 03/09/2007
BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER

BERTAGNA, ANGELA MARIE

ART UNIT

PAPER NUMBER

1637

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
--	-----------	---------------

3 MONTHS

03/09/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/522,171	Applicant(s) PEDERSEN ET AL.	
	Examiner Angela Bertagna	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4,7-9,14,22,26-28,33-36,38-43,53,54 and 57-60 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,7-9,14,22,26-28,33-36,38-43,53,54 and 57-60 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>6/1/06; 1/27/06; 11/4/05</u> | 6) <input type="checkbox"/> Other: ____ |

Art Unit: 1637

DETAILED ACTION

Remarks

1. Claims 3, 5, 6, 10-13, 15-21, 23-25, 29-32; 37, 44-52, 55, 56, and 61 have been canceled by a preliminary amendment filed November 4, 2005. Accordingly, claims 1, 2, 4, 7-9, 14, 22, 26-28, 33-36, 38-43, 53, 54, and 57-60 are currently pending and will be examined on the merits.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

3. The information disclosure statement filed June 1, 2006 has not been considered, because it appears to be a duplicate of the IDS filed January 27, 2006. The references cited on the IDS filed June 1, 2006 have been considered in the earlier-filed IDS (see attached PTO-1449). Similarly, WO 91/05058 and WO 05/026387 have been cited twice on the IDS filed November 4, 2005. The duplicative citations have been lined through. Also, reference AZ (Salas et al. Journal of Biological Chemistry (1968)) cited on the IDS filed November 4, 2005, has not been considered, because a complete copy of the article has not been provided.

Art Unit: 1637

Specification

4. The disclosure is objected to because of the following informalities: Nucleic acid sequences greater than 10 nucleotides in length appear on pages 54 and 56 of the specification. These sequences must be identified by the appropriate SEQ ID numbers.

Appropriate correction is required.

Claim Objections

5. Claim 54 is objected to because of the following informalities: This claim is missing a period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 38 and 39 are indefinite, because claim 38 recites the limitation "the nick(s)" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Art Unit: 1637

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 2, 9, 14, 22, 26-28, 33, 38, 39, 41, 42, 54, and 57-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Stemmer (US 6,117,679).

Regarding claim 1, Stemmer teaches a method for preparing a template switched product encoded by at least part of one first template and at least part of at least one second template, wherein said product comprises at least one predetermined property (see columns 27-28, “Parallel PCR” section), comprising:

(i) providing a first template molecule and at least one second template molecule (column 27, lines 53-55)

(ii) providing a nucleic acid polymerase (column 27, lines 58-59; see also column 10, lines 15-21)

(iii) synthesising a plurality of different template switched products by contacting sequentially in any order, or simultaneously, at least part of the first template and at least part of the at least one second template with said polymerase under conditions allowing for template dependent nucleotide polymerization (column 27, lines 53-59)

wherein the synthesis of each individual template switched product involves at least one template switch (column 27, lines 59-65), and

wherein the synthesis of the plurality of different template switched products involves a plurality of template switches (column 24, lines 20-25 and lines 48-49)

(iv) separating at least one template switched product comprising the at least one predetermined property from said plurality of template switched products (column 28, lines 1-4)

(v) obtaining a template switched product comprising at least one predetermined property (column 28, lines 1-6).

Regarding claim 2, Stemmer teaches that in the method of claim 1:

(i) the first template comprises a first activity or encodes a molecule comprising a first activity

(ii) the second template comprises a second activity or encodes a molecule comprising a second activity

(iii) the predetermined property of the template switched product is a third activity, either comprised within the template switched product or in a molecule encoded by the template switched product; and wherein the first and second activities are both different from the third activity (see column 7, lines 55-67, where Stemmer teaches shuffling of different viral proteins to generate novel epitopes; see also column 8, lines 1-12, where Stemmer teaches shuffling of nucleic acids encoding different polypeptides to generate enzymes with novel activities).

Regarding claim 9, Stemmer teaches that the polymerase comprises reverse transcriptase activity (column 10, lines 18-21).

Regarding claim 14, Stemmer teaches that the first template and/or the second template are nucleic acid molecules (column 27, lines 53-59).

Regarding claim 22, Stemmer teaches that the first template and/or the second template are RNA molecules (column 22, lines 51-52).

Art Unit: 1637

Regarding claims 26-28 and 33, Stemmer teaches introducing into said first and/or second template one or more template switch signals prior to synthesis of the template switched product, specifically breaks in the template (column 23, lines 18-21), predetermined secondary structure (column 23, lines 49-52 – the recombination junctions), or nucleotide analogues (column 26, lines 49-67, especially lines 64-67).

Regarding claims 38, 39, and 41, Stemmer teaches introduction of nick(s) by limited enzymatic digestion with a ribonuclease (column 23, lines 24-26). Stemmer also teaches limited fragmentation using hydroxyl radicals (column 31, lines 19-25).

Regarding claim 42, Stemmer teaches addition of one or more factors capable of affecting frequency and/or degree and/or accuracy of template switching (column 10, lines 15-18).

Regarding claim 54, Stemmer teaches that in the method of claim 1, the one or more templates have been prepared by a method comprising the steps of:

- (i) providing a RNA molecule (column 22, lines 51-52)
- (ii) fragmenting said RNA molecule into RNA fragments (column 23, lines 24-26)
- (iii) replicating one or more of said RNA fragments (column 26, lines 21-39)
- (iv) thereby obtaining one or more different templates (column 26, lines 21-3).

Regarding claims 57 and 58, Stemmer teaches amplification of the template switched products by PCR (column 27, lines 58-65).

Regarding claims 59 and 60, Stemmer teaches that the method of claim 1 is repeated at least once, wherein template switched product(s) are used as a first template and/or second template when the method is repeated (column 26, lines 8-20).

Art Unit: 1637

9. Claims 1, 4, 8, 9, 14, 26, 27, 38, and 57-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (Proceedings of the National Academy of Sciences, USA (1997) 94: 4504-4509) as evidenced by Stemmer (Proceedings of the National Academy of Sciences, USA (1994) 91: 10747-10751) and Jones et al. (Nucleic Acids Research (1989) 17(20): 8387-8388).

Regarding claim 1, Zhang teaches a method for preparing a template switched product encoded by at least part of one first template and at least part of at least one second template, wherein said product comprises at least one predetermined property, comprising:

(i) providing a first template molecule and at least one second template molecule (see Figure 1, where a pool of random DNA fragments are provided)

(ii) providing a nucleic acid polymerase (see Figure 1, where reassembly PCR is taught; see also page 10747 “PCR without primers” section of the 1994 Stemmer reference, cited by Zhang at page 4505, column 1, which teaches that the reassembly PCR is conducted using Taq polymerase)

(iii) synthesising a plurality of different template switched products by contacting sequentially in any order, or simultaneously, at least part of the first template and at least part of the at least one second template with said polymerase under conditions allowing for template dependent nucleotide polymerization (see Figure 1, where the family of related sequences produced by reassembly PCR are template-switched products; see also page 4504, column 2, where Zhang teaches that reassembly PCR generates template-switched products)

wherein the synthesis of each individual template switched product involves at least one template switch (page 4505, column 2), and

wherein the synthesis of the plurality of different template switched products involves a plurality of template switches (page 4504, column 2)

(iv) separating at least one template switched product comprising the at least one predetermined property from said plurality of template switched products (Figure 1, where Zhang teaches screening of individual products; see also page 4505, column 2)

(v) obtaining a template switched product comprising at least one predetermined property (page 4505, column 2).

Regarding claim 4, Zhang teaches that the method of claim 1 involves more than two different template switches (page 4504, column 2).

Regarding claim 8, Zhang teaches that the method involves providing in a single reaction mixture more than 10 different templates and obtaining more than 100 different template switched products (see page 4505, column 2, where Zhang teaches conducting the reaction using 20-40 templates obtained from the first round of shuffling in a second round of shuffling and obtaining approximately 10,000 products).

Regarding claim 9, Zhang teaches that the polymerase comprises reverse transcriptase activity (see page 4505, column 1, where Zhang teaches conducting the reassembly PCR using the method taught in the Stemmer 1994 reference. Stemmer teaches at page 10747 that Taq DNA polymerase is used for reassembly; Jones teaches at page 8387 that Taq DNA polymerase possesses reverse transcriptase activity).

Regarding claim 14, Zhang teaches that the first template and/or the second template are nucleic acid molecules (see Figure 1).

Art Unit: 1637

Regarding claims 26, 27, and 38, Zhang teaches introducing into said first and/or second template one or more template switch signals prior to synthesis of the template switched product, specifically enzymatically induced breaks in the template (see Figure 1, where Zhang teaches random fragmentation; see also page 10747 of the 1994 Stemmer reference, cited by Zhang at page 4505, column 1, which teaches that this fragmentation occurs by DNase I digestion).

Regarding claims 57 and 58, Zhang teaches amplification of the template switched products by PCR (see page 10747 of the 1994 Stemmer reference, cited by Zhang at page 4505, column 1, which teaches PCR amplification of the products).

Regarding claims 59 and 60, Zhang teaches that the method of claim 1 is repeated at least once, wherein template switched product(s) are used as a first template and/or second template when the method is repeated (see Figure 1 and page 4505, column 2).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

Art Unit: 1637

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer (US 6,117,679) in view of Svarovskaia et al. (Journal of Virology (2000) 74(15): 7171-7178; cited on IDS).

Stemmer teaches the method of claim 1, as discussed above.

Stemmer teaches conducting the shuffling reaction under conditions that promote template switching and suggests addition of a reverse transcriptase to the reaction (column 10, lines 15-25), but does not teach that the reverse transcriptase comprises an RNase H activity.

Svarovskaia analyzed a number of mutations in MMLV reverse transcriptase in order to determine the contribution of different regions of the enzyme to template switching frequency (see abstract). Svarovskaia reported that all mutations in the RNase H domain halved the observed frequency of template switches (Table 1 on page 7174). Based on these data as well as previous observations, Svarovskaia determined that the RNase H activity of this reverse transcriptase was essential for a high frequency of template switches (page 7175, column 2).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to include a reverse transcriptase with RNase H activity in the shuffling method taught by Stemmer. As noted above, Stemmer expressly taught that the shuffling reaction should be conducted under conditions that promoted template switching and further suggested including a reverse transcriptase in the reaction (column 10, lines 15-25). Since Svarovskaia taught that the RNase H activity of MMLV-RT was essential to obtaining a high frequency of template switches

Art Unit: 1637

(see abstract, Table 1, and page 7175, column 2), an ordinary practitioner would have been motivated to use this reverse transcriptase in the method of Stemmer in order to promote a high degree of template switching. Therefore, the combined teachings of Stemmer and Svarovskaia result in the method of claim 7.

12. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer (US 6,117,679 in view of Gaur et al. (FEBS Letters (1993) 315(1): 56-60) and further in view of DeStefano et al. (Journal of Virology (1992) 66(11): 6370-6378).

Stemmer teaches the method of claim 33, as discussed above.

Stemmer teaches the use of nucleotide analogues (column 26, lines 49-67), but does not teach the use of analogues that cannot be incorporated into a nucleic acid.

Gaur teaches enzymatic synthesis of RNA using nucleotide analogues (see abstract).

Gaur teaches that an analog of dGTP could not be incorporated into the nascent RNA by RNA polymerase (see abstract and page 60).

DeStefano analyzed the requirements for strand transfer by reverse transcriptase and determined that pausing of the enzyme enhances strand transfer (see abstract).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to utilize a nucleotide analog that cannot be incorporated into nucleic acids in the method of Stemmer. Stemmer expressly taught modification of reaction conditions to increase strand transfer frequency (column 10, lines 15-25) and further taught use of analogs (column 26, lines 49-67). Since DeStefano taught that polymerase pausing increased the strand transfer frequency (see abstract), an ordinary practitioner would have been motivated to utilize any agent

Art Unit: 1637

known to result in polymerase pausing in order to increase the frequency of strand transfer, such as the dGTP analog taught by Gaur. An ordinary practitioner would have recognized that the dGTP analog of Gaur would result in polymerase pausing when bound to the polymerase since it could not be incorporated into the nascent nucleic acid, and polymerization would only resume upon its diffusion away from the polymerase. Therefore, an ordinary practitioner of the method taught by Stemmer, interested in promoting strand transfer by increasing polymerase pausing, would have been motivated to add a nucleotide analog unable to be incorporated into a nucleic acid, as suggested by the teachings of Gaur and DeStefano, thus resulting in the instantly claimed method.

13. Claims 35 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer (US 6,117,679) in view of Chenchik et al. (US 5,994,076).

Stemmer teaches the method of claim 33, as discussed above.

Regarding claim 53, Stemmer teaches a method comprising:

- (i) providing a DNA molecule (column 22, lines 51-52)
- (ii) providing a mixture of nucleotides and nucleotide analogs (column 26, lines 49-67)
- (iii) contacting the DNA molecule with the mixture and transcribing or replicating the DNA, thereby obtaining one or more different templates (column 26, line 49 – column 27, line 1).

Stemmer teaches the use of nucleotide analogues (column 26, lines 49-67), but does not teach the use of analogs that prohibit further elongation.

Chenchik teaches a method of analyzing differential gene expression using a “CAPswitch” oligonucleotide that undergoes template switching to amplify cDNA (see abstract and column 9, lines 9-25 for a general description).

Regarding claims 35 and 53, Chenchik teaches that the use of nucleotide analogs, such as chain terminators, improve the efficiency of template switching (column 9, lines 42-51).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to utilize a chain terminating nucleotide analog in the method of Stemmer. Stemmer expressly taught modification of reaction conditions to increase strand transfer frequency (column 10, lines 15-25) and further taught use of analogs (column 26, lines 49-67). Since Chenchik taught that chain-terminating analogs improved the efficiency of template switching, an ordinary practitioner would have been motivated to include a chain terminator in the reaction, in order to promote template switching, as suggested by Stemmer. An ordinary practitioner would have had a reasonable expectation of success in doing so, since Stemmer taught the use of analog-containing templates in the shuffling method (column 26, lines 49-67). Therefore, an ordinary practitioner of the shuffling method taught of Stemmer, interested in promoting strand transfer as suggested by Stemmer, would have been motivated to include at least one chain terminating nucleotide analog in the reaction, as suggested by Chenchik, thus resulting in the instantly claimed methods.

14. Claims 36 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer (US 6,117,679) in view of Chenchik et al. (US 5,962,272) and further in view of Gish et al. (Science (1988) 240: 1520-1522).

Art Unit: 1637

Stemmer teaches the method of claims 27 and 43, as discussed above.

Stemmer does not teach the use of phosphorothioated ribonucleotides in the reaction.

Stemmer also does not teach fragmentation of nucleic acids using alkaline hydrolysis.

Chenchik teaches a method of analyzing differential gene expression using a “CAPswitch” oligonucleotide that undergoes template switching to amplify cDNA (see abstract and column 9, lines 9-25 for a general description).

Regarding claim 36, Chenchik teaches that the use of nucleotide analogs, including backbone analogs, improve the efficiency of template switching (column 9, lines 42-51).

Chenchik does not teach phosphorothioated ribonucleotides.

Gish teaches a method of sequencing DNA or RNA. Regarding claims 36 and 40, Gish taught that RNA substituted with phosphorothioated ribonucleotides was more efficiently cleaved by alkaline hydrolysis (page 1520, column 1).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to utilize a phosphorothioated ribonucleotide in the method taught by Stemmer. Stemmer expressly taught modification of reaction conditions to increase strand transfer frequency (column 10, lines 15-25) and further taught use of analogs (column 26, lines 49-67) and fragmented nucleic acids (column 23, lines 18-29). Since Chenchik taught that nucleotide analogs, including backbone analogs, increased the frequency of template switching (column 9, lines 42-51), an ordinary practitioner would have been motivated to substitute template nucleic acids with any known analog, such as the phosphorothioated ribonucleotides taught by Gish, recognizing their functional equivalence. Furthermore, since Gish taught that phosphothiesters were more efficiently cleaved by alkaline reagents than phosphodiester (page 1520, column 1),

Art Unit: 1637

an ordinary practitioner would have been motivated to incorporate phosphorothioated nucleotides in order to more efficiently obtain fragmented templates for shuffling by the method of Stemmer. Regarding claim 40, it also would have been obvious for an ordinary artisan to fragment the nucleic acids using any known fragmentation method. Stemmer taught fragmentation by chemical, enzymatic, or physical means (column 23, lines 18-29), but did not specify alkaline hydrolysis. Since Gish taught fragmentation using alkaline hydrolysis (page 1520, column 1), an ordinary practitioner would have recognized that alkaline hydrolysis was a functional equivalent of the fragmentation methods taught by Stemmer. Therefore, the method of claims 36 and 40 is prima facie obvious in view of the combined teachings of Stemmer, Chenchik, and Gish.

15. Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer (US 6,117,679) in view of DeStefano et al. (Journal of Virology (1992) 66(11): 6370-6378) and further in view of Mandiyan et al. (Nucleic Acids Research (1990) 18(23): 7055-7062).

Stemmer teaches the method of claim 42, as discussed above.

Stemmer does not teach that DMS, kethoxal, DEPC, or CMCT is used to increase the frequency of template switching.

DeStefano analyzed the requirements for strand transfer by reverse transcriptase and determined that pausing of the enzyme enhances strand transfer (see abstract).

Mandiyan teaches that treatment of RNA with DMS, kethoxal, DEPC, or CMCT results in modification of unpaired bases (abstract and page 7056, column 2). Mandiyan further teaches

Art Unit: 1637

that the presence of these chemically-modified bases causes pausing by reverse transcriptase (page 7056, column 2).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to promote template switching in the method of Stemmer by inclusion of DMS, kethoxal, DEPC, or CMCT in the reaction mixture. Stemmer taught conducting the method under conditions that promoted strand switching (column 10, lines 15-25). Since DeStefano taught that pausing of reverse transcriptase increased the frequency of strand transfer (abstract), an ordinary practitioner would have been motivated to conduct the shuffling reaction of Stemmer under conditions that resulted in polymerase pausing. Since Mandiyan taught treatment of RNA with DMS, kethoxal, DEPC, CMCT produced chemically modified nucleotides that induced polymerase pausing (page 7056, column 2), an ordinary practitioner would have been motivated to include any of these reagents in the reaction mixture to increase polymerase pausing, and thereby, increase the frequency of template switching, as suggested by Stemmer. Thus, one of ordinary skill in the art, interested in promoting template switching, as suggested by Stemmer, would have been motivated to induce polymerase pausing, as suggested by DeStefano, by including DMS, kethoxal, CMCT, or DEPC in the reaction mixture, as suggested by Madiyan, thus resulting in the instantly claimed method.

Conclusion

No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela Bertagna whose telephone number is 571-272-8291. The examiner can normally be reached on M-F, 7:30 - 5.


Art Unit: 1637

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Angela Bertagna
Examiner, Art Unit 1637
March 1, 2007

amb


GARY BENZION, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600